REMARKS

Restriction:

In the April 28, 2005 Office Action the Examiner required restriction to one of the following groups under 35 U.S.C. §121:

Group I: Claims 1-57, 97-115, and 116-117, drawn to neutralizing antibodies and to a method of making;

Group II: Claims 58-79, and 118, drawn to a method of neutralizing botulinum neurotoxin A (BoNT/A);

Group III: Claims 80-96, drawn to polypeptides.

In addition, the Examiner required election of a species (sequence) from Tables 4, 9, or 11, and a single species (clone) from S25, C25, C39, 1C6, 1F3, 3D12, B4, huC25, Ar11, Ar2, WR1(V), WR1(T), 3-1, 3-8, 3-10, ING for initial examination.

In response to this restriction requirement, Applicants elect Group I, claims 1-57, 97-115, and 116-117.

With respect to the election of species, Applicant elect clone huC25 (SEQ ID NOS: 86 + 87 + 88 + 89 + 126 + 127 + 128 (VH) and SEQ ID NOs: 156 + 157 + 158 + 159 + 196 + 197 + 198 (VL)).

It is noted that the huC25 VH domain is a combination of SEQ ID NOS: 86-89 + 126-128, while the huC25 VL domain is a combination of SEQ ID NOS: 156-159 + 196-198.

With respect to the elected species, it is noted that claims 1, 3, 8, 17-57, 97, 99, 104, 113-117 read on the elected species.

Sequence Compliance.

The Examiner alleged that at page 8, lines 12 and 14, sequences which contain more than 4 amino acids are set forth that do not evidence a sequence identifier (SEQ ID NO). **In the preliminary amendment filed on April 12, 2004 (accompanying the sequence listing), page 8, lines 12 and 14 were amended to provide sequence identifiers.**

The Examiner alleged that Table 4 sets forth a plurality of amino acid sequencwes which must have sequence identifiers assigned and inserted. **In the preliminary amendment filed on April 12, 2004 (accompanying the sequence listing), a replacement Table 4 contaiing the required SEQ ID NOs was provided**. For the purposes of clarity, however, a clearer replacement Table 4 is provided herewith.

The Examiner alleged that at page 85, Table 11, clone huC25 is missing three SEQ iD NOs. **This row of Table 11 is carried over to page 86, where the SEQ ID Numbers are provided (see page 86, line 1).**

The Examiner alleged that at page 86, Table 11, clone huC25 is missing four SEQ iD NOs. **This row of Table 11 is carred over to page 87, where the SEQ ID Numbers are provided (see page 87, line 1).**

In view of the foregoing, Applicants believe the application is in compliance with the sequence listing rules.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Table 4. Deduced protein sequences of V_H and V_L of BoNT/A Hc binding scFv classified by epitope recognized.

V_H Region Epitope	Clone	Lib	Framework 1 / Framework 3	CDR1	Framework 2 / CDR3	CDR2 / Framework 4	SEQ ID NO.
1	C15	1	QVJLQQSGAELVRPGASVKLSCKTSGYSFT / MATLTVDKSSSTAYMQLSSPTSEDSAVYYCAR	SYWMN	WVKQGPGQGLEWIG / GIYYDYDGGNYYAMDY	MIHPSNSEIRFNQKFED / WGQGTTVTASS	48
	C9	1	-------------------------------- / ----------------------------------	-----	------V------- / ----------------	----------------N / -----V--	49
	1D5	2	E---VE-------------------------- / K--------------N----A----	-----	--------R------ / ----------------	-------T-L---K- / --L-V----	50
	C1	1	-----------------K---- / -----K------IH----	-----	--------R------ / -L-GYGF WYFDV	----------DT / ---V----	51
	S25	1	-----------------K---- / -----K------T----L	-----	--------R------A----L / -L-GNGF WYF-V	-----D-DT / ---V----	52
	1B6	2	--Q--------------K----- / --V---I--A--T-I-N--E-ARL-D--I-	D-A-H	----------S-AKS RGKG / V-SSYYGDTDY-I-KG	WYF-V / ---V----	53
	1C9	2	E-Q-K------------K----- / --V---I--A--T-I-N--N--E-PRL-	D-AVH	--------SHAKS RGKG / V-STYYGDTDY-PK-KG / S--V--		54
	1E8	2	--Q-K------------K----- / RISI-R-T-KNQFFL-N-V-T--TGT-	D-AW-	-IR-F-KK---N -YD / Y-S YSGSTGYNPSLKS	/ S--V--	55
	1G7	2	--Q-K------------K----- / RISI-R-T-KNQFFL-N-V-T--TGT-	D-AWY	-IR-F-KK---N -YD / Y-S YSGSTGYNPSLKS	/ ---S--V--	56
2	1A1	2	EVKLVESGGGLVQPGGSRKLSCATSGFTFS / RFTISRDNAKNTLYLQMSSLKSEDTAMYYCVR	DYYMS	WIRQSPDKRLEWVA / HGYGNYPSH WYFDV	TISDGGTYTYPDSVKG / WGAGTTVTVSS	57
	1F1	2	-V-----------A---------S-	N-G--	--V--T------Y / M-S-S-N-S-		58
	C39	1	Q-Q-Q---S-K----L----A------	-----	--V-T-E------ / -S-	----S---- / -Y----Q-	59
	C25	1	Q-Q-Q------K----L----A----N-	-----	-V-T-E------ YR-DEGK / -S-	----S---- / -Y----Q-	60
	2G5	2	--------K----L----A-----HN-	S-A--	-V-T-E------ YR-DDAM / ---S-	/ -Y----Q-S-- T-N----	61
	3C3	2	----K---K----L----A-----HN-	S-A--	-V-T-E------ NLPYDHV / -A-	/ -Y----Q-S-- T-N----	62
	3F4	2	EG---------K----L----A-----HN-	S-A--	-V-T-EH------ NLPYDHV / -A-	----F---T-N---- / -Y----Q-S--	63
	3H4	2	----------K--PL----A-----HN-	S-A--	-V-T-EH------ NLPYDHV / -A-	----F---T-N---- / -Y----Q-S--	64
3	1B3	2	EVQLQESGGGBVVQPGRSLRLSCAASGFTF / RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR	SYAMH	WVRQAPGKGLEWVA DWSEGYYYYG / VISYDGSNKYYADSVKG MDV	WGQGTTVIVSS	65
	1C6	2	QI--LQ-------------------				66
	2B6	2	VKLVESGP-L-KPSQSLSLTCTVTGYSIT- / -ISIT-T---QFF-KL-VTS--T-----	D-AWN	-I--F--NK---MG / AGDGY-VD WYFDV	Y-N-----N-NP -L-N / --T-----	67

-1-

V_H Region (continued) — group 4

Name	No.	Sequence	SEQ ID NO
1G5	2	Q-----Q--AEL----A-VKM-K---Y--T --WTT --K-R--Q-----IG D-YPGSGSTNYNEKF-S KA-LTV-T-SS-A-M-LS--TS-----S----- ELGD A---Y ------S-----	68
1H6	2	---K-A-VKM-K---Y--T --WTT --K-R--Q-----IG D-YP-SGSTNYNEKF-S KA-LTV-T-SS-A-M-LS--TS-----S----- ELGD A---Y ------S-----	69
1F3	2	EVQLQQSGAELVKPGASVKLSCKASGYTFT SFWMH WVKQRPGRGLEWIG RLDPNSGETKYNEKFKS KATLTVDKPSSTAYMELSSLTSEDSAVYYCAR EAYGYWN FDV WGTGTTVTVSS	70
2E8	2	------------------------- --K-----	71

V_L Region

Header (row 1): Framework 1 | CDR1 | Framework 2 | CDR2
Header (row 2): Framework 3 | CDR3 | Framework 4

Name	No.	Sequence	SEQ ID NO
2C15	1	DIELTQSPAIMSASPGEKVIMTC SASS SVSHMY WYQQKPGSSPRLLIY DTSNLAS GVPIRFSGSGSGTSYSLTISRMEAEDSATYYC QQWSSYPFT FGSGTKLELKR	72
C9	1	--D-------- --S------ ---Y-H -F------T-KPW- S----- --Y-G--L ---A-----I-	73
1D5	2	--A-------I- ---S I-S-NLH ------SV-A- G----- --V ---S-A- -YG-----I-	74
C1	1	---V ----Y- ---L- --A----- --A-	75
S25	1	----------L-A- ---V--S I-S-NLH --S-T-KPW- G----- --V ---L- ---A-----I-	76
1B6	2	--------SLAV-L-QRA-IS- RA-ESVDSYGN-F-H ---QP-K--- RA----E- --I-A------R-DFT--INPV--D-V--- --SNED-P- --A-----	77
1C9	2	--------SLAV-L-QRA-IS- RA-ESVDSYGN-F-H ---QP-K--- RA----E- --I-A------R-DFT--NPV--D-V--- --SNED-Y- --G-----I-	78
1E8	2	---Y-H --S-T-KRW- ---K--- --A- ----N-L- ---A-----	79
1G7	2	---Y-H --S-T-KRW- ---K--- --A- ----N-L- ---A-----	80
1A1	2	DIELTQSPASLAVSLGQRATISC RASESVDSYGNSFMH WYQQKPGQPPKLLTY LASNLES GVPARFSGSGSRTDFTLTIDFVEADDAATYYC QQNNEDPYT FGGGTKLEIKR	81
1F1	2	--T-------- --------- ---------	82
C39	1	---R------ ---H --------- ---- ----------	83
C25	1	--I-------G------ ---H--Q R------P --N----V- -S------	84
2G5	2	----IMSA-P-EKVTTT- S--S SV-Y- -F-----TS-K-W- ST---A- --G-SYS---SRM-E- --RSSY--- -S-----F-	85
3C3	2	----IMSA-P-EKVTTT- ---H--Q -F-----TS-K-W- ----DQAGN-S --G-SYS---SRM-E- --RSSY---	86
3F4	2	-T------IMSA-P-EKVTMT- S--S SV-Y-Y --SS-R----- DT---A- --V------G-SYS---SRM-E- --WSSY-P-	87
3H4	2	----IMSA-P-EKVTMT- ---S VSS-YL- --SS-R----- DT---A- --V------G-SYS---SRM-E- --WSSY-P-	88

3	1B3	2	DSELTQSPTTMAASPGEKITTTC SASSS ISSNYLH WYQQRPGFSPKLLIY RTSNLAS GVPARFSGSGSGTSYSLTIGTMEAEDVATYYC QQGSSIPRT FGGGTKLEIKR	89
	1C6	2	-I------ASL-V-L-RRA--S- R--E-VEYYGTSLMQ ----K--QP------ AA--VE- -------------DF--N=HPV-E -I-M-F- --SRKV-W- ---------	90
	2B6	2	YI------ASL-V-L-QRA--S- R--E-VDSYGNSFM- ----K--QP------ LA---E- -------------R-DFT---DPV--D-A----- --NED-Y- ---------S	91
	1G5	2	-I------ASL-V-L-QRA--S- R--E-VEYYGTSLMQ ----K--QP------ AA--VE- -A----------DF--N-HPV-ED-I-M-F- --SRKV-Y- ---------	92
	1H6	2	-I------AI-S------V----- ---SN-- ----KS-T----W--- G------ ---V-----------------SS-----A----- --W--Y-L- --A---V-LR-	93
4	1F3	2	DIELTQSPASMSASPGEKVTMTC RATSS VSSSYLH WYQQKSGASPKLWIY SASNLAS GVPSRFSGSGSGTSYSLTISSVEAEDAATYYC QQYIGYPYT FGGGTKLEIKR	94
	2E8	2	-------TT-A------I-I-- S-S-- IG-N-- ------P-F----L--- RT----- ---A-------------GAM----V------ --GSSI--- ---------	95